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Personality and resilience to Alzheimer's disease neuropathology: A prospective autopsy study

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Abstract

Alzheimer's disease (AD) neuropathology is found at autopsy in about 30% of cognitively normal older individuals. We examine whether personality traits are associated with such resilience to clinical dementia in individuals with AD neuropathology. Broad factors and specific facets of personality were assessed up to 28 years (M=11, SD=7) before onset of dementia and up to 30 years (M=15, SD=7) before death in a cohort (N=111) evaluated for AD neuropathology at autopsy. Individuals with higher baseline scores on vulnerability to stress, anxiety, and depression (neuroticism: OR=2.0, 95%CI=1.2-3.5), or lower scores on order and competence (conscientiousness: OR=0.4, 95%CI=0.2-0.9) were less likely to remain asymptomatic in the presence of AD neuropathology. Neuroticism (r=0.26), low agreeableness (r=-0.34), and some facets were also significantly associated with advanced stages of neurofibrillary tangles, but the associations between personality traits and risk of clinical dementia were mostly unchanged by controlling for Braak and CERAD scores. In sum, a resilient personality profile is associated with lower risk or delay of clinical dementia even in persons with AD neuropathology.

Keywords

Alzheimer's disease; dementia; asymptomatic; personality; neuroticism; depression; conscientiousness; prospective cohort study; autopsy; neurofibrillary tangles; A β neuritic plaques; neuropathology

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Introduction

Among cognitively normal individuals older than 75 years, about one-third has sufficient neuritic plaques and neurofibrillary tangles at autopsy to meet criteria for Alzheimer's disease (AD) (Arriagada et al. 1992; Bennett et al. 2006a; Driscoll and Troncoso 2011). These cases, referred to as asymptomatic AD (ASYMAD) or high pathology controls, can be informative to understand the progression of the disease and to help identify factors that promote cognitive resilience, or cognitive reserve (Bennett et al. 2006b; Craik et al. 2010; Fratiglioni et al. 2004; Iacono et al. 2009; Tucker and Stern 2011).

In this study, we investigate whether personality traits contribute to the cognitive resilience of ASYMAD compared to those with both clinical dementia and corresponding AD pathology at autopsy. A number of studies indicate that those who score higher on conscientiousness and lower on neuroticism engage in fewer health-risk behaviors and have healthier metabolic, cardiovascular, and inflammatory risk profiles (Chapman et al. 2011; Courneya and Hellsten 1998; Deary et al. 2010; Sutin et al. 2010; Sutin et al. 2010; Sutin et al. 2011; Terracciano and Costa 2004; Terracciano et al. 2008; Wilson et al. 2004). Prospective studies indicate that cognitively normal older adults who score higher on conscientiousness or lower on neuroticism have a lower risk of developing clinical symptoms of AD (Duberstein et al. 2011; Wilson et al. 2003; Wilson et al. 2005; Wilson et al. 2007). These traits were unrelated to the extent of neuropathologic damage at autopsy (Wilson et al. 2003; Wilson et al. 2007), which suggests that personality traits may offset the effects of AD-like brain pathology. We test this hypothesis by examining whether personality traits predict who is cognitively resilient (ASYMAD) and who is not (AD) in the face of AD neuropathology found at autopsy. Thus, we specifically compare the pre-clinical personality traits of those who subsequently developed clinical dementia with those who subsequently died cognitively normal but with AD neuropathology at autopsy. We also examine whether personality traits are associated with semiquantitative measures of neuritic plaques and neurofibrillary tangles.

Methods

BLSA Study and Autopsy Program

Subjects were participants in the autopsy program of the Baltimore Longitudinal Study of Aging (BLSA). The BLSA is a prospective study of physical and psychological aging (Shock et al. 1984). To date 519 participants have enrolled into the autopsy component of the study, of which 267 died and 224 were examined at autopsy and had complete clinical and neuropathology data. The interval between the last clinical evaluation and autopsy was $M = 0.95$ year, $SD = 1.04$. Personality data were missing for 16 participants that died or developed dementia before they had a chance to complete the questionnaire, and an additional 12 cases were excluded because personality was assessed in the year of dementia's onset or after. Although we included all available cases in secondary analyses, we excluded 85 participants from the primary analyses according to the criteria described below. The primary analyses were thus based on up to 111 participants who completed the personality inventory at least once prior to onset of cognitive impairment. The larger proportion of males (75 men, 68%) in the sample reflects the composition of the BLSA cohort, which was limited to men until 1978. All participants analyzed in this study were of European ancestry.

Participants agreed to serial follow-ups until their death, gave written informed consent prior to each assessment, and assented to autopsy. Final autopsy consent was obtained from the next-of-kin or legally designated individual. The local institutional review board and the NIA approved all BLSA protocols and the associated autopsy program.

Clinical and Neuropsychological evaluations of the BLSA

Baseline evaluations for each participant enrolled into the BLSA autopsy study were performed by a neurologist to document history of cerebrovascular disease, focal neurological abnormalities, and impairment of cognitive or behavioral functions due to secondary causes or medical treatments. Follow-up evaluations included a neuropsychological battery, neurological examination, medication review, and informant/subject structured interview. The latter was based on the Clinical Dementia Rating (CDR) (Morris 1997) scale after 1998 and the Dementia Questionnaire (Kawas et al. 1994) prior to 1998. All subjects were reviewed at a diagnostic consensus conference if their Blessed Information Memory Concentration score (Blessed et al. 1968) was 4 or above, if their informant or subject CDR score was 0.5 or above, or if their Dementia Questionnaire was abnormal. All subjects, regardless of the screening tests, were evaluated at a diagnostic conference at the time of entry into the autopsy program and at withdrawal or death. Personality data were not considered at the diagnostic conference, where the full panel of neuropsychological diagnostic tests and clinical data were available for review. Diagnosis of dementia was based on DSM-III-R criteria and diagnosis of AD was based on the National Institute of Neurological and Communication Disorders and Stroke-Alzheimer's Disease and Related Disorders Association (NINCDSADRDA) criteria (McKhann et al. 1984).

Personality traits assessment

Personality traits were assessed in 1980 and 1986 using the NEO Personality Inventory (NEO-PI) and from 1989 using the Revised NEO Personality Inventory (NEO-PI-R) (Costa and McCrae 1992). The NEO-PI-R is a 240-item questionnaire that assesses 30 facets, six for each of the five major dimensions of personality – Neuroticism, Extraversion, Openness, Conscientiousness, and Agreeableness. The NEO-PI did not assess the conscientiousness and agreeableness domains; therefore the analyses for these two domains were based on the subsample tested with the full NEO-PI-R. The neuroticism, extraversion, and openness domains were measured with essentially identical scales in the NEO-PI and NEO-PI-R. Raw scores were standardized using combined-sex norms (Costa and McCrae 1992). The NEO instruments have been extensively validated in the BLSA and other samples. In the BLSA sample, the NEO-PI-R factor structure shows high congruence with the normative structure (Tucker's ϕ 's = .97 to .99) and the internal consistencies for the five dimensions range from 0.87 to 0.92. As reported elsewhere (Terracciano et al. 2006), over an average interval of 19 years the test-retest correlations between the 1980 NEO-PI and later NEO-PI-R assessments were 0.73, 0.74, and 0.77 for neuroticism, extraversion, and openness, respectively. These dimensions are thus highly reliable and stable (Terracciano et al. 2006).

Neuropathology methods and diagnostic criteria

All brains were examined at the Alzheimer's Disease Research Center of the Johns Hopkins University. After weighing and external examination, the right hemisphere was cut in 1-cm coronal slabs and frozen at -80°C. The left hemisphere was fixed in 10% buffered formaldehyde for at least 2 weeks and then cut coronally. For diagnostic purposes, tissue blocks were dissected from middle frontal gyrus, superior and middle temporal gyri, inferior parietal cortex, occipital cortex, entorhinal cortex, amygdala, thalamus, basal ganglia and cerebellum. Tissue blocks were processed and embedded in paraffin, cut at 10 μ m, and stained with hematoxylin-eosin (H&E) and Hirano-silver method (Yamamoto and Hirano 1986) for diagnostic purposes. The severity of neuritic plaques (NP) was assigned a semiquantitative score of 0 for none, A or 1 for rare, B or 2 for moderate, and C or 3 for frequent, according to the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) criteria (Mirra et al. 1991), except we did not adjust for age. The neurofibrillary tangles (NFT) stage was assigned a score (0 to 6) according to Braak (Braak and Braak

1991, 1998). Vascular lesions (infarcts, lacunes, and hemorrhages) were evaluated on all H&E-stained sections.

Because of the small sample sizes of subjects with mild cognitive impairment due to AD, we excluded these individuals from analyses. Similarly, we excluded dementia cases with other primary neuropathological processes, including vascular disease, fronto-temporal dementia, Lewy-Body dementia, and cases in which clinical dementia assessment might have been compromised by psychiatric or other pathologies, including intraparenchymal hemorrhages and primary or metastatic brain tumors. Lewy body disease was determined on immunostain findings of α -synuclein lesions (Lewy bodies or neurites; anti- α -synuclein antibody from BD Transduction laboratories, Biosciences, Palo Alto, CA; dilution 1:500) in brainstem or cerebral cortex and tauopathies were determined by anti-phosphorylated tau (PHF-1 clone; a gift of Dr. P. Davies, Albert Einstein College of Medicine, Bronx, NY; dilution 1:100).

Definition of study groups

Based on the clinical diagnosis within the last year of life and the neuropathology evaluation, the participants were divided into three groups:

Normal—The Control subjects had no history of cognitive and/or behavioral deficits or cerebrovascular disease. On neuropathology evaluation, the brains showed no or rare A β neuritic plaques on Hirano silver stains. Accordingly, the CERAD NP score was 0 or A. Neurofibrillary changes were confined to transentorhinal, entorhinal cortex and hippocampus; thus their Braak NFT scores ranged between 0 and 2.

Asymptomatic Alzheimer's disease (ASYMAD)—The ASYMAD subjects had no history of behavioral deficits or cerebrovascular disease and were cognitively intact through the last cognitive and physical evaluation within one year before death. On neuropathology evaluation, the brains showed diffuse and A β neuritic plaques, CERAD scores were B or C. The NFT Braak scores were 2 or higher.

Alzheimer's disease (AD)—The AD subjects were patients who received a clinical diagnosis of dementia according to the DSM-III-R criteria and of probable AD according to the NINDS-ADRDA criteria (McKhann et al., 1984). The average age of AD onset was 83 years (SD = 8). The neuropathologic examination of these subjects showed A β neuritic plaques with CERAD scores B to C, and NFT with Braak stages 2 or higher. The brains were free of other potential causes of cognitive decline.

Statistics

We used logistic regressions to test whether personality traits (scaled in 1 SD units) were associated with increased risk of manifesting clinical dementia vs. remaining asymptomatic in the presence of AD neuropathology. We included in the model age at death, sex, and educational levels as covariates because older age, being female, and lower education are associated with increased risk of dementia. We also included the time interval between personality assessment and onset of dementia or death for those who died cognitively normal. We repeated the analyses including the Braak and CERAD scores as additional covariates. We also repeated the analyses excluding cases that completed the personality questionnaire within 5 years of the onset of clinical dementia, to reduce potential bias in self-assessed traits with approaching cognitive impairment (Ruby et al. 2009). Because neuroticism and conscientiousness are associated with BMI (BMI = kg/m²) (Sutin et al. 2011; Magee and Heaven 2011) and cigarette smoking (ever smoked) (Terracciano and Costa 2004), which are risk factors for dementia (Daviglus et al. 2010; Barnes and Yaffe 2011), we examined BMI and ever smoking as covariates and potential mediators. Finally

we examined whether personality traits were associated with Braak and CERAD scores, controlling for the above covariates.

Results

The analyses were based on up to 111 participants who completed the personality questionnaire at least once. Based on the clinical, neurological, and cognitive assessments, and the pathological findings at autopsy, participants were classified as normal (n=27), ASYMAD (n=29), or AD (n=55). Table 1 shows demographic, clinical, and neuropathology information for the three groups. Compared to the AD, the ASYMAD had fewer A β neuritic plaques (CERAD, $p < 0.01$), fewer neurofibrillary tangles (Braak, $p < 0.01$) and died at a relatively younger age ($p = 0.02$). There were no significant differences at baseline on age, BMI, or ever smoking ($p > 0.05$).

The baseline personality assessment was obtained 1 to 28 years ($M = 11$, $SD = 7$) before onset of dementia and 1 to 30 years ($M = 15$, $SD = 7$) before death. Table 2 presents the average personality scores at baseline for the normal, ASYMAD, and AD groups. The ASYMAD scored about one-half SD lower on neuroticism compared to AD and normal. The AD scored about one-half SD lower on conscientiousness compared to the normal and ASYMAD (Figure 1). Logistic regressions (Table 2) indicated that scoring 1 SD higher on neuroticism ($OR = 2.00$, $95\%CI = 1.15-3.49$) or 1 SD lower on conscientiousness ($OR = 0.43$, $95\%CI = 0.21-0.88$) was associated with about twofold higher risk of incident clinical dementia among those with AD neuropathology. Analyses at the facet level indicated that those who scored lower on anxiety, depression, and vulnerability to stress, or higher on assertiveness, order and competence were significantly more likely to remain asymptomatic despite the presence of AD neuropathology (Table 2).

To examine whether the associations were influenced by personality traits assessed close to dementia onset, we repeated the analyses excluding 12 cases that completed the baseline questionnaire within 5 years of the onset of clinical dementia. The association remained significant for neuroticism ($OR = 2.03$, $95\%CI = 1.10-3.77$) and conscientiousness ($OR = 0.41$, $95\%CI = 0.19-0.91$), and for the anxiety, vulnerability to stress, competence, and order facets ($p < 0.05$). The associations were also essentially the same when controlling for BMI and cigarette smoking, and we found no evidence that BMI and ever smoking mediated the association between personality traits and risk of dementia.

Because the AD group had more neuropathology than the ASYMAD, we repeated the analyses including Braak and CERAD as covariates. We again found that scoring higher on neuroticism ($OR = 2.03$, $95\%CI = 1.01-4.12$) or lower on conscientiousness ($OR = 0.38$, $95\%CI = 0.15-0.93$) was associated with higher risk of incident clinical dementia. The associations were also significant for the depression, vulnerability to stress, assertiveness, modesty, competence, and self-discipline facets ($p < 0.05$). We further tested but found no significant interactions between the five major factors and CERAD and Braak scores in predicting clinical dementia.

We combined the AD and ASYMAD groups to examine whether personality traits were associated with the semiquantitative measure of the severity of A β neuritic plaques (CERAD) and the stage of neurofibrillary tangles (Braak). None of the five factors were associated with the CERAD score (Table 3). Higher scores on neuroticism and lower scores on agreeableness were associated with higher stages of neurofibrillary tangles. Higher Braak scores were particularly found in those more anxious and hostile, and in those who scored lower on the trust, straightforwardness, compliance, and deliberation facets.

Finally, we examined whether the above results generalized to dementia due to non-AD pathology (e.g. vascular) and cases with mixed etiology. We found no mean differences between the subjects with dementia due to AD vs. other causes on neuroticism or conscientiousness ($p > .05$). Logistic regression indicated that scoring higher on neuroticism ($OR = 1.86$, $95\%CI = 1.14-3.03$) or lower on conscientiousness ($OR = 0.50$, $95\%CI = 0.28-0.90$) was associated with higher risk of developing clinical dementia.

Comment

In this study we found that greater emotional resilience and conscientiousness were associated with reduced risk of developing clinical dementia in subjects with AD neuropathology. More precisely, asymptomatic individuals with AD pathology scored lower on neuroticism, vulnerability to stress, anxiety, and depression compared to both old controls and those who developed clinical dementia. The asymptomatic did not differ significantly from controls on conscientiousness, but low scores on this trait and the order and competence facets were found in the group that developed clinical dementia, both AD and all-cause dementia. These results suggest that low neuroticism increases resilience while low conscientiousness increases vulnerability to clinical dementia. Both traits could represent a resource for individuals to cope with brain pathology or delay the onset of clinical dementia.

In prospective studies, both neuroticism and conscientiousness predict who is at greater risk of developing AD versus remaining cognitively normal (Duberstein et al. 2011; Wilson et al. 2003; Wilson et al. 2005; Wilson et al. 2007). Our findings are consistent with these previous studies and provide novel evidence that these same traits are predictive of clinical dementia among the more restricted group that are found at autopsy to have AD neuropathology.

Individuals who are more emotionally stable and conscientious may have greater resilience to neuropathology, in part, because they are generally healthier (Chapman et al. 2011; Cuijpers et al. 2010; Deary et al. 2010; Ozer and Benet-Martinez 2006) and engage in behaviors and lifestyles associated with a reduced risk of dementia (Barnes and Yaffe 2011; Daviglus et al. 2010; Fratiglioni et al. 2004). For example, those who score low on neuroticism and high on conscientiousness are more likely to exercise and less likely to be obese or smoke (Courneya and Hellsten 1998; Sutin et al. 2011; Terracciano and Costa 2004). In the current study, however, neither BMI nor ever smoking mediated the relation between personality and risk of clinical dementia. Emotionally stable and conscientious individuals also have more favorable metabolic and inflammatory risk profiles (Sutin et al. 2010; Sutin et al. 2010) and they are less likely to report depressive symptoms or to suffer from depression (Kendler et al. 2006; Weiss et al. 2009), which have all been linked to risk of clinical dementia (Dotson et al. 2008; Saczynski et al. 2010). Personality traits are also related to coping strategies, and difficulty with stress management over the lifespan has been associated with changes in hippocampal function and structure (McEwen 1999; Warner-Schmidt and Duman 2006). Both low neuroticism and high conscientiousness have also been related to larger volume of the prefrontal and medial temporal regions and with less decline with advancing age (Jackson et al. 2011). Finally, low neuroticism is also associated with higher levels of serum brain derived neurotrophic factors (BDNF) (Lang et al. 2004; Terracciano et al. 2011), a key protein in synaptic neurogenesis thought to play a role in neurodegenerative diseases (Nagahara et al. 2009).

Personality might also be related to the severity and spread of neuropathology. Although we found no association of the five factors with the semiquantitative measure of A β neuritic plaques, we found that high neuroticism and low agreeableness were associated with more

advanced spread of tangles in limbic and neocortical regions, as indexed by Braak staging. Low trust (cynical, skeptical) and low straightforwardness (manipulative, deceptive) were the only facets associated with both the severity of A β neuritic plaques and the stage of neurofibrillary tangles. These associations might be due to the less favorable metabolic, cardiovascular, and inflammatory profile of those scoring low on these agreeableness facets (Sutin et al. 2010, 2010, 2011). Some previous studies have not found an association between quantitative measures of neuropathology and personality traits (Wilson et al. 2003; Wilson et al. 2007), whereas others have found higher levels of cortical tangle formations in AD patients to be associated with comorbid depression (Rapp et al. 2008) and aggressive behaviors (Lai et al. 2010).

This study has several strengths, including the longitudinal design, the autopsy of study participants, and the detailed assessment of the five major dimensions of personality and 30 specific facets. Although long term prospective studies coupled with autopsy evaluations are rare, the potential selective attrition and the relatively small sample size are limitations of this study, as is the non-representativeness of the sample. For example, clinical dementia was unrelated to education, most likely due to restricted range given the generally high level of education within the BLSA sample.

The association between personality traits and increased vulnerability to clinical dementia might have implications for clinical trials (Duberstein et al. 2011). Similar to education, personality traits might contribute to defining the population at risk. Personality traits might also moderate intervention efficacy, such that some interventions might be more or less effective depending on level of anxiety, and traits such as order might be particularly relevant for adherence to behavioral and pharmacologic treatments.

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Figure 1. Neuroticism and Conscientiousness scores in normal, asymptomatic (ASYMAD), and symptomatic Alzheimer's Disease (AD)

Table 1

Demographic information and neuropathology in three groups.

	Normal (n=27)	ASYMAD (n=29)	AD (n=55)	P [*]
Age, ^a y	65.5 (13.4)	72.3 (10.2)	72.5 (11.0)	.91
Age death, y	78.0 (9.4)	85.4 (7.7)	89.4 (6.7)	.017
Time to death, ^a y	12.6 (7.1)	13.1 (6.5)	16.8 (7.6)	.029
Education, y	17.6 (2.0)	17.6 (2.0)	17.7 (2.3)	.83
Women, n (%)	3 (11%)	9 (31%)	24 (44%)	.26
Ever smoked, n (%)	18 (66%)	13 (45%)	32 (58%)	.24
BMI	26.4 (5.1)	25.8 (4.7)	24.7 (3.5)	.21
CERAD	0.3 (0.4)	2.2 (0.4)	2.5 (0.5)	.007
Braak	1.7 (0.5)	3.5 (1.0)	4.7 (1.1)	<.001

AD= Alzheimer's disease; ASYMAD = Asymptomatic subjects with Alzheimer's neuropathology at autopsy; CERAD = Consortium to Establish a Registry for Alzheimer's Disease (0 = none, 1 = rare, 2 = moderate, 3 = frequent); BMI = Body Mass Index.

^a Age and MMSE at first Revised NEO Personality Inventory assessment, and time from the first personality assessment to death.

* The P value is from a t-test between AD and ASYMAD.

Table 2

Mean personality traits at baseline in three groups.

	Normal	ASYMAD	AD	OR (95% CI) ^a
Neuroticism	48.9 (9)	45.2 (9)	50.5 (10)	2.00 (1.15-3.49)*
Extraversion	42.5 (8)	49.2 (10)	45.7 (10)	0.68 (0.41-1.12)
Openness	49.1 (9)	51.1 (10)	51.5 (10)	1.03 (0.58-1.82)
Agreeableness	49.6 (9)	51.9 (6)	51.4 (8)	0.75 (0.38-1.49)
Conscientiousness	49.7 (6)	50.6 (10)	43.7 (9)	0.43 (0.21-0.88)*
N1: Anxiety	48.3 (11)	45.2 (9)	50.9 (12)	2.15 (1.18-3.93)*
N2: Angry Hostility	47.5 (10)	46.7 (10)	48.7 (11)	1.20 (0.74-1.95)
N3: Depression	50.0 (11)	48.0 (9)	51.8 (9)	1.93 (1.08-3.47)*
N4: Self-consciousness	49.9 (7)	45.6 (8)	50.3 (10)	1.62 (0.97-2.72)
N5: Impulsiveness	48.4 (10)	45.9 (8)	47.6 (9)	1.27 (0.75-2.13)
N6: Vulnerability	50.9 (10)	46.7 (7)	53.0 (10)	2.46 (1.30-4.67)*
E1: Warmth	45.5 (8)	49.9 (10)	48.8 (9)	0.84 (0.52-1.36)
E2: Gregariousness	43.9 (9)	51.3 (11)	47.6 (9)	0.66 (0.40-1.10)
E3: Assertiveness	51.1 (9)	53.6 (10)	48.9 (10)	0.53 (0.31-0.93)*
E4: Activity	45.3 (9)	49.3 (11)	48.5 (10)	0.87 (0.53-1.44)
E5: Excitement-Seeking	42.2 (8)	46.2 (9)	44.0 (10)	0.83 (0.51-1.35)
E6: Positive Emotions	41.8 (8)	46.6 (8)	45.3 (10)	0.88 (0.53-1.45)
O1: Fantasy	48.8 (9)	46.9 (10)	47.9 (9)	1.16 (0.70-1.92)
O2: Aesthetics	48.9 (11)	52.9 (8)	53.8 (10)	1.03 (0.59-1.82)
O3: Feelings	47.7 (9)	49.3 (9)	51.1 (10)	1.30 (0.79-2.13)
O4: Actions	47.8 (10)	51.2 (9)	50.0 (10)	0.79 (0.43-1.45)
O5: Ideas	54.2 (9)	53.5 (9)	50.8 (11)	0.66 (0.38-1.15)
O6: Values	48.0 (7)	50.0 (10)	51.8 (11)	1.32 (0.76-2.28)
A1: Trust	54.0 (8)	57.0 (6)	53.7 (8)	0.38 (0.14-1.06)
A2: Straightforwardness	49.5 (13)	51.5 (7)	52.7 (8)	0.90 (0.39-2.08)
A3: Altruism	51.1 (11)	47.9 (10)	48.7 (7)	1.03 (0.48-2.19)
A4: Compliance	48.8 (9)	55.6 (9)	53.7 (11)	0.48 (0.22-1.05)
A5: Modesty	47.0 (10)	45.5 (7)	47.6 (9)	2.02 (0.84-4.89)
A6: Tender-mindedness	48.0 (13)	49.4 (7)	48.7 (9)	1.02 (0.48-2.15)
C1: Competence	53.1 (6)	51.0 (9)	44.9 (9)	0.38 (0.16-0.89)*
C2: Order	45.4 (7)	48.7 (9)	41.1 (10)	0.41 (0.20-0.85)*
C3: Dutifulness	52.8 (10)	52.5 (7)	50.3 (7)	0.44 (0.16-1.18)
C4: Achievement Striving	47.7 (9)	49.9 (10)	48.5 (9)	0.93 (0.43-1.98)
C5: Self-Discipline	45.5 (7)	48.4 (10)	40.9 (11)	0.58 (0.31-1.07)
C6: Deliberation	53.8 (8)	51.1 (9)	46.5 (9)	0.53 (0.26-1.07)

Note. AD= Alzheimer's disease; ASYMAD = Asymptomatic subjects with Alzheimer's neuropathology at autopsy. Means (Standard Deviations) for the four groups. N = 111 for the neuroticism, extraversion, and openness domains and facets; N = 73 for agreeableness and conscientiousness domains and facets

^aOR (odd ratios) and 95% Confidence Interval comparing AD to ASYMAD, controlling for age of death, sex, time interval since personality assessment, and education. * P < 0.05

Table 3

Personality traits associations with semiquantitative measure of neuritic plaques (CERAD) and neurofibrillary tangle stages (Braak).

	CERAD	Braak
Neuroticism	.03	.26 *
Extraversion	-.08	.03
Openness	.02	.02
Agreeableness	-.18	-.34 *
Conscientiousness	.03	-.23
N1: Anxiety	.14	.33 *
N2: Angry Hostility	-.05	.28 *
N3: Depression	-.06	.13
N4: Self-consciousness	.07	.08
N5: Impulsiveness	-.08	.10
N6: Vulnerability	.09	.19
E1: Warmth	.02	-.06
E2: Gregariousness	.00	-.01
E3: Assertiveness	-.08	.01
E4: Activity	.01	.14
E5: Excitement-Seeking	-.26 *	.01
E6: Positive Emotions	.02	.05
O1: Fantasy	.00	.04
O2: Aesthetics	-.02	.00
O3: Feelings	.10	.03
O4: Actions	-.02	.00
O5: Ideas	-.01	.05
O6: Values	.04	-.07
A1: Trust	-.39 *	-.38 *
A2: Straightforwardness	-.29 *	-.39 *
A3: Altruism	.00	.01
A4: Compliance	-.04	-.27 *
A5: Modesty	.03	-.16
A6: Tender-mindedness	.13	.02
C1: Competence	-.09	-.13
C2: Order	.06	-.26
C3: Dutifulness	-.10	-.23
C4: Achievement Striving	.33 *	.05
C5: Self-Discipline	.11	-.07
C6: Deliberation	-.17	-.33 *

Note. Partial correlations between personality traits and neuritic plaques (CERAD) and tangles (Braak) controlling for age of death, time interval since personality assessment, sex, and education in the sample of ASYMAD and AD (n = 84 for the neuroticism, Extraversion, and Openness domains and facets; N = 59 for agreeableness and Conscientiousness domains and facets).

*
P < 0.05

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